

## REMARKS

Claims 1-4, 6-8, 10, and 12-17 are in the present application.

### 1. Rejections over Essenfeld, et al. under 102(e)

The Examiner repeated her rejection of Claims 1-4, 6, 13, 14 and 16 under 35 U.S.C. §102(e) as allegedly anticipated by Essenfeld, et al. Applicants respectfully submit that Essenfeld, et al, does not anticipate the presently claimed invention.

Claim 3 has been cancelled.

Claim 1 as currently amended in this response recites a DMSO concentration of greater than 20%. Essenfeld, et al., do not disclose a DMSO concentration of greater than 20%. Column 16, lines 13-45, cited in the Final Rejection, discloses a solution of 40% isopropyl alcohol, 40% acetone, 20% polyethylene glycol and 1% DMSO. In fact, every Example disclosed by Essenfeld, et al., teaches a DMSO concentration of only 1%. Accordingly, since Essenfeld, et al., does not disclose every element of the present claims, Applicants respectfully submit that the rejection under §102(e) should be withdrawn.

### 2. Rejections over Essenfeld under 35 U.S.C. §103(a)

The rejection over Essenfeld, et al., of Claims 7, 8, 10 and 17 under 35 U.S.C. §103(a) was maintained. Applicants respectfully submit that the present invention is not obvious over Essenfeld, et al.

Essenfeld, et al. teaches only DMSO concentrations of one percent (1%). Each of Examples 1 through 3 of Essenfeld, et al., teach use of DMSO at one percent (1%). In contrast, each of Claims 7, 8, 10 and 17 of the present invention recite DMSO concentrations of greater than 20%. It is respectfully submitted that a concentration *twenty times (20x) greater* than that taught by Essenfeld is not obvious to one of ordinary skill in the art.

The Examiner stated that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum by routine experimentation. However, the only general condition or range taught by Essenfeld is a single concentration of 1%. The rejected claims recite a concentration of 20% which lies 20-times out of that range.

Further, the prior art teaches away from increasing the DMSO concentration to greater than 20%. See "A Guide to the Properties and Uses of Detergents in Biology and Biochemistry," Judith Neugebauer, CALBIOCHEM Corporation (1988) (copy of relevant pages attached) (hereinafter referred to as "Neugebauer"). Essinfeld, et al., includes DMSO as a surfactant (see column 5, Line 24). Neugebauer teaches that detergents, which includes surfactants (see pg. 4), will solubilize membranes at detergent:protein ratios from 10:1 to 0.1:1 (see pg. 17). Thus, Neugebauer teaches that a DMSO:protein ratio of 0.1:1 will solubilize a tissue sample. Since Essinfeld, et al., considers preservation of morphology to be critical, a person of ordinary skill in the art would not have been motivated to increase DMSO concentration to 20%.

Neugebauer also teaches that some detergents will interfere with staining or fixing procedures (see pg. 16). Accordingly, since Essinfeld, et al., relates to fixation of tissues, a person of ordinary skill in the art would be motivated to minimize the amount of DMSO used. A person of ordinary skill in the art would not have been motivated to increase DMSO concentration 20-times.

Accordingly, it is respectfully submitted that the rejection of Claims 7, 8, 10 and 17 under 35 U.S.C. §103(a) should be withdrawn.

### 3. Rejections over Essinfeld in view of Evinger-Hodges under 35 U.S.C. §103(a)

Claim 15 was rejected under 35 U.S.C. §103(a) as being unpatentable over Essinfeld et al. in view of Evinger-Hodges, et al. (WO 90/02204). Applicant's traverse.

Claim 15 depends from Claim 1. Claim 1 recites a DMSO concentration of greater than 20%. As stated above, Essinfeld, et al., neither teaches nor suggests the presently claimed invention. Evinger-Hodges neither teaches nor otherwise suggests a DMSO concentration of greater than 20%. Accordingly, it is respectfully submitted that the rejection of Claim 15 under 35 U.S.C. §103(a) should be withdrawn.

#### 4. Rejections over Essenfeld in view of Rogers under 35 U.S.C. §103(a)

Claim 12 was rejected under 35 U.S.C. §103(a) as being unpatentable over Essenfeld et al. in view of Rogers. Applicant's traverse.

Claim 12 depends from Claim 1. Claim 1 recites a DMSO concentration of greater than 20%. As stated above, Essenfeld, et al., neither teaches nor suggests the presently claimed invention.

Applicants respectfully submit that it is Rogers is improperly cited as prior art. The Federal Circuit has held that "In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the invention was concerned." *In re Oetike*, 977 F.2d 1443, 1446 (Fed. Cir. 1992) Rogers describes a method to clarify and contrast intact biological tissue samples for microscopic analysis. Such a method is not in the field of the present Applicant's endeavor to stabilize nucleic acids. In fact, the USPTO classified Rogers as belonging to Class 435, Subclass 40.5. In contrast, the USPTO classified the present invention in Class 536. Thus, the USPTO patent classification system states that Rogers is not in the field of Applicant's endeavor.

Nor is Rogers reasonably pertinent. A person of ordinary skill in the art, interested in nucleic acid stabilization, would not logically look to a reference relating a method to clarify and contrast stain intact biological tissue samples for microscopic analysis. See *Wang Labs v. Toshiba Corp.*, 993 F.2d 858 (Fed. Cir. 1993) ("A reference is reasonably pertinent if, even though it may be in a different field from that of the inventor's endeavor, it is one which, because of the matter with which it deals, logically would have commended itself to an inventor's attention in considering his problem.") The solution cited by the Examiner is a fixative solution (for preparing cells for microscopic analysis). A person of ordinary skill in the art, interested in nucleic acid stabilization, would not logically consider fixative solutions for microscopy in considering an answer to her molecular problem.

Furthermore, the method of Rogers is not limited to the methanol and DMSO solution cited by the Examiner at Column 5 Line 50 through Column 6, Line 3. The method taught by Rogers also includes very low temperatures (-70°C), gentle agitation, application of a vacuum in cycles, use of hydrogen peroxide, use of 100% methanol, use of pigment, use of a benzyl


alcohol/benzyl benzoate solution, mounting, use of fresh BABB solution and viewing the specimen under a microscope. See Column 5, Line 62 through Column 6, Line 48. It is respectfully submitted that a person of ordinary skill in the art would not view this rather extensive method for viewing a specimen under a microscope as reasonably pertinent to her problem of nucleic acid stabilization. Nor would a person of ordinary skill, interested in nucleic acid stabilization, be motivated to focus upon a small portion of the overall non-analogous method taught by Rogers.

Accordingly, it is respectfully submitted that the rejection of Claims 12 under 35 U.S.C. §103(a) should be withdrawn.

### CONCLUSIONS

The claims of the present application are believed to be in condition for allowance, and early notice thereof is respectfully requested.

Respectfully submitted,



Allan M. Kiang  
Attorney for the Applicant  
Registration No. 42,275

Becton Dickinson and Company  
1 Becton Drive  
Franklin Lakes, New Jersey 07416  
(201) 847-7111

doc#63003